

Amendments to the Claims

1. - 46. (Canceled)

47. (Previously Presented) A multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) composition for oral administration comprising two quantities of particles, each of the particles comprising

- (i) an inert non-pareil core,
- (ii) an SSRI layer comprising fluvoxamine or a pharmaceutically-acceptable salt thereof disposed over the inert core, and
- (iii) a coating of a rate-controlling polymeric acrylate, methacrylate lacquer, or a mixture thereof disposed over the fluvoxamine,

wherein the composition allows the controlled release of the fluvoxamine over a period of not less than about 12 hours following oral administration, wherein the rate-controlling polymeric acrylate or methacrylate lacquer coating of the first quantity of particles is present in a first amount, and the rate-controlling polymeric acrylate or methacrylate lacquer coating of the second quantity of particles is present in a second amount that is different from the first amount, and wherein the fluvoxamine release rate from the composition exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

- (a) no more than about 15% of the total fluvoxamine is released after 0.5 of an hour of measurement in the apparatus;
- (b) no more than about 25% of the total fluvoxamine is released after 1 hour of measurement in the apparatus;
- (c) between about 20% and 75% of the total fluvoxamine is released after 2 hours of measurement in the apparatus;
- (d) not less than about 75% of the total fluvoxamine is released after 4 hours of measurement in the apparatus; and
- (e) not less than about 85% of the total fluvoxamine is released after 6 hours of measurement in the apparatus.

48. (Previously Presented) The composition according to Claim 47 wherein the coating is the polymeric acrylate lacquer.

49. (Previously Presented) The composition according to Claim 47 wherein the coating is the methacrylate lacquer.

50. (Previously Presented) The composition according to Claim 47 wherein the coating is a lacquer which contains a mixture of acrylate and methacrylate.

51. (Previously Presented) The composition according to Claim 47 wherein the coating is an acrylic resin comprising a copolymer of acrylic and methacrylic acid esters having a low content of quaternary ammonium groups.

52. - 54. (Canceled)

55. (Previously Presented) The composition of Claim 47 wherein the rate-controlling coating comprises an ammonio methacrylate lacquer and a plasticizer, the combined amount of the ammonio methacrylate lacquer and the plasticizer in the membrane coating being in an amount of from about 4% to about 15% of the weight of the particle.

56. (Previously Presented) The composition of Claim 55 wherein the combined amount of the ammonio methacrylate lacquer and the plasticizer in the rate controlling coating of the first or second quantity of particles is in an amount of 4%, 6%, 8%, 10%, 12%, or 15% of the weight of the particle.

57. (Previously Presented) A method for the treatment of depression or obsessive compulsive disorder treatable with an SSRI, comprising administering to a patient suffering from one of the conditions a therapeutically effective amount of a multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) composition for oral administration comprising two quantities of particles, each of the particles comprise

(i) an inert non-pareil core,

(ii) an SSRI layer comprising fluvoxamine or a pharmaceutically-acceptable salt thereof disposed over the inert core, and

(iii) a coating of a rate-controlling polymeric acrylate, methacrylate lacquer, or a mixture thereof disposed over the fluvoxamine,

wherein the composition allows the controlled release of the fluvoxamine over a period of not less than about 12 hours following oral administration, and wherein the rate-controlling polymeric acrylate or methacrylate lacquer coating of the first quantity of particles is present in a first amount, and the rate-controlling polymeric acrylate or methacrylate lacquer coating of the second quantity of particles is present in a second amount that is different from the first amount, and wherein the fluvoxamine release rate from the composition exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

(a) no more than about 15% of the total fluvoxamine is released after 0.5 of an hour of measurement in the apparatus;

(b) no more than about 25% of the total fluvoxamine is released after 1 hour of measurement in the apparatus;

(c) between about 20% and 75% of the total fluvoxamine is released after 2 hours of measurement in the apparatus;

(d) not less than about 75% of the total fluvoxamine is released after 4 hours of measurement in the apparatus; and

(e) not less than about 85% of the total fluvoxamine is released after 6 hours of measurement in the apparatus.

58. - 61. (Canceled)

62. (Currently Amended) The composition of Claim 47, wherein the controlled-release of the fluvoxamine is effective in supplying fluvoxamine to the blood of a patient such that, following a single application of the composition to the patient, the amount of circulating fluvoxamine ( $AUC_{0-\infty}$ ) in the blood serum of the patient is about 128 to about 1,175 ng/ml.h.

63. - 81. (Canceled)

82. (New) A multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) composition for oral administration comprising two quantities of particles, each of the particles comprising

(i) an inert non-pareil core,

(ii) an SSRI layer comprising fluvoxamine or a pharmaceutically-acceptable salt thereof disposed over the inert core, and

(iii) a coating of a rate-controlling polymeric acrylate, methacrylate lacquer, or a mixture thereof disposed over the fluvoxamine,

wherein the composition allows the controlled release of the fluvoxamine over a period of not less than about 12 hours following oral administration, wherein the rate-controlling polymeric acrylate or methacrylate lacquer coating of the first quantity of particles is present in a first amount, and the rate-controlling polymeric acrylate or methacrylate lacquer coating of the second quantity of particles is present in a second amount that is different from the first amount, and wherein the fluvoxamine release rate from the composition exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

- (a) no more than about 20% of the total fluvoxamine is released after 4 hours of measurement in the apparatus;
- (b) no more than about 45% of the total fluvoxamine is released after 6 hours of measurement in the apparatus;
- (c) between about 45% and 80% of the total fluvoxamine is released after 8 hours of measurement in the apparatus;
- (d) not less than about 70% of the total fluvoxamine is released after 10 hours of measurement in the apparatus; and
- (e) not less than about 80% of the total fluvoxamine is released after 12 hours of measurement in the apparatus.

83. (New) The composition of Claim 82, wherein the coating is the polymeric acrylate lacquer.

84. (New) The composition of Claim 82, wherein the coating is the methacrylate lacquer.

85. (New) The composition of Claim 82, wherein the coating is a lacquer which contains a mixture of acrylate and methacrylate.

86. (New) The composition of Claim 82, wherein the coating is an acrylic resin comprising a copolymer of acrylic and methacrylic acid esters having a low content of quaternary ammonium groups.

87. (New) The composition of Claim 82, wherein the rate-controlling coating comprises an ammonio methacrylate lacquer and a plasticizer, the combined amount of the ammonio methacrylate lacquer and the plasticizer in the membrane coating being in an amount of from about 4% to about 15% of the weight of the particle.

88. (New) The composition of Claim 82, wherein the combined amount of the ammonio methacrylate lacquer and the plasticizer in the rate controlling coating of the first or second quantity of particles is in an amount of 4%, 6%, 8%, 10%, 12%, or 15% of the weight of the particle.

89. (New) The composition of Claim 82, wherein the controlled-release of the fluvoxamine is effective in supplying fluvoxamine to the blood of a patient such that, following a single application of the composition to the patient, the amount of circulating fluvoxamine ( $AUC_{0-\infty}$ ) in the blood serum of the patient is about 128 to about 1,175 ng/ml.h.

90. (New) A multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) composition for oral administration comprising two quantities of particles, each of the particles comprising

- (i) an inert non-pareil core,
- (ii) an SSRI layer comprising fluvoxamine or a pharmaceutically-acceptable salt thereof disposed over the inert core, and
- (iii) a coating of a rate-controlling polymeric acrylate, methacrylate lacquer, or a mixture thereof disposed over the fluvoxamine,

wherein the composition allows the controlled release of the fluvoxamine over a period of not less than about 12 hours following oral administration, wherein the rate-controlling polymeric acrylate or methacrylate lacquer coating of the first quantity of particles is present in a first amount, and the rate-controlling polymeric acrylate or methacrylate lacquer coating of the second quantity of particles is present in a second amount that is different from the first amount, and wherein the fluvoxamine release rate from the composition exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

- (a) no more than 20% of the total fluvoxamine is released after 1 hour of measurement in the apparatus;
- (b) no more than 60% of the total fluvoxamine is released after 2 hours of measurement in the apparatus;
- (c) not less than 20% of the total fluvoxamine is released after 4 hours of measurement in the apparatus;
- (d) not less than 35% of the total fluvoxamine is released after 6 hours of measurement in the apparatus;
- (e) not less than 50% of the total fluvoxamine is released after 8 hours of measurement in the apparatus;
- (f) not less than 70% of the total fluvoxamine is released after 10 hours of measurement in the apparatus; and
- (g) not less than 75% of the total fluvoxamine is released after 12 hours of measurement in the apparatus.

91. (New) The composition of Claim 90, wherein the coating is the polymeric acrylate lacquer.

92. (New) The composition of Claim 90, wherein the coating is the methacrylate lacquer.

93. (New) The composition of Claim 90, wherein the coating is a lacquer which contains a mixture of acrylate and methacrylate.

94. (New) The composition of Claim 90, wherein the coating is an acrylic resin comprising a copolymer of acrylic and methacrylic acid esters having a low content of quaternary ammonium groups.

95. (New) The composition of Claim 90, wherein the rate-controlling coating comprises an ammonio methacrylate lacquer and a plasticizer, the combined amount of the ammonio methacrylate lacquer and the plasticizer in the membrane coating being in an amount of from about 4% to about 15% of the weight of the particle.

96. (New) The composition of Claim 90, wherein the combined amount of the ammonio methacrylate lacquer and the plasticizer in the rate controlling coating of the first or second quantity of particles is in an amount of 4%, 6%, 8%, 10%, 12%, or 15% of the weight of the particle.

97. (New) The composition of Claim 90, wherein the controlled-release of the fluvoxamine is effective in supplying fluvoxamine to the blood of a patient such that, following a single application of the composition to the patient, the amount of circulating fluvoxamine ( $AUC_{0-x}$ ) in the blood serum of the patient is about 128 to about 1,175 ng/ml.h.

98. (New) A multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) composition for oral administration comprising two quantities of particles, each of the particles comprising

- (i) an inert non-pareil core,
- (ii) an SSRI layer comprising fluvoxamine or a pharmaceutically-acceptable salt thereof disposed over the inert core, and
- (iii) a coating of a rate-controlling polymeric acrylate, methacrylate lacquer, or a mixture thereof disposed over the fluvoxamine,

wherein the composition allows the controlled release of the fluvoxamine over a period of not less than about 12 hours following oral administration, wherein the rate-controlling polymeric acrylate or methacrylate lacquer coating of the first quantity of particles is present in a first amount, and the rate-controlling polymeric acrylate or methacrylate lacquer coating of the second quantity of particles is present in a second amount that is different from the first amount, and wherein the fluvoxamine release rate from the composition exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

- (a) no more than about 20% of the total fluvoxamine is released after 1 hour of measurement in the apparatus;
- (b) no more than about 45% of the total fluvoxamine is released after 2 hours of measurement in the apparatus;

(c) between about 20% and about 70% of the total fluvoxamine is released after 4 hours of measurement in the apparatus;

(d) between about 35% and about 85% of the total fluvoxamine is released after 6 hours of measurement in the apparatus;

(e) not less than about 50% of the total fluvoxamine is released after 8 hours of measurement in the apparatus;

(f) not less than about 70% of the total fluvoxamine is released after 10 hours of measurement in the apparatus; and

(g) not less than about 75% of the total fluvoxamine is released after 12 hours of measurement in the apparatus.

99. (New) The composition of Claim 98, wherein the coating is the polymeric acrylate lacquer.

100. (New) The composition of Claim 98, wherein the coating is the methacrylate lacquer.

101. (New) The composition of Claim 98, wherein the coating is a lacquer which contains a mixture of acrylate and methacrylate.

102. (New) The composition of Claim 98, wherein the coating is an acrylic resin comprising a copolymer of acrylic and methacrylic acid esters having a low content of quaternary ammonium groups.

103. (New) The composition of Claim 98, wherein the rate-controlling coating comprises an ammonio methacrylate lacquer and a plasticizer, the combined amount of the ammonio methacrylate lacquer and the plasticizer in the membrane coating being in an amount of from about 4% to about 15% of the weight of the particle.

104. (New) The composition of Claim 98, wherein the combined amount of the ammonio methacrylate lacquer and the plasticizer in the rate controlling coating of the first or second quantity of particles is in an amount of 4%, 6%, 8%, 10%, 12%, or 15% of the weight of the particle.

105. (New) The composition of Claim 98, wherein the controlled-release of the fluvoxamine is effective in supplying fluvoxamine to the blood of a patient such that, following a single application of the composition to the patient, the amount of circulating fluvoxamine ( $AUC_{0-\infty}$ ) in the blood serum of the patient is about 128 to about 1,175 ng/ml.h.

106. (New) A multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) composition for oral administration comprising two quantities of particles, each of the particles comprising

- (i) an inert non-pareil core,
- (ii) an SSRI layer comprising fluvoxamine or a pharmaceutically-acceptable salt thereof disposed over the inert core, and
- (iii) a coating of a rate-controlling polymeric acrylate, methacrylate lacquer, or a mixture thereof disposed over the fluvoxamine,

wherein the composition allows the controlled release of the fluvoxamine over a period of not less than about 12 hours following oral administration, wherein the rate-controlling polymeric acrylate or methacrylate lacquer coating of the first quantity of particles is present in a first amount, and the rate-controlling polymeric acrylate or methacrylate lacquer coating of the second quantity of particles is present in a second amount that is different from the first amount, and wherein the fluvoxamine release rate from the composition exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

- (a) no more than about 50% of the total fluvoxamine is released after 2 hours of measurement in the apparatus;
- (b) not less than about 35% of the total fluvoxamine is released after 6 hours of measurement in the apparatus; and
- (c) not less than about 80% of the total fluvoxamine is released after 22 hours of measurement in the apparatus.

107. (New) The composition of Claim 106, wherein the coating is the polymeric acrylate lacquer.

108. (New) The composition of Claim 106, wherein the coating is the methacrylate lacquer.

109. (New) The composition of Claim 106, wherein the coating is a lacquer which contains a mixture of acrylate and methacrylate.

110. (New) The composition of Claim 106, wherein the coating is an acrylic resin comprising a copolymer of acrylic and methacrylic acid esters having a low content of quaternary ammonium groups.

111. (New) The composition of Claim 106, wherein the rate-controlling coating comprises an ammonio methacrylate lacquer and a plasticizer, the combined amount of the ammonio methacrylate lacquer and the plasticizer in the membrane coating being in an amount of from about 4% to about 15% of the weight of the particle.



112. (New) The composition of Claim 106, wherein the combined amount of the ammonio methacrylate lacquer and the plasticizer in the rate controlling coating of the first or second quantity of particles is in an amount of 4%, 6%, 8%, 10%, 12%, or 15% of the weight of the particle.

113. (New) The composition of Claim 106, wherein the controlled-release of the fluvoxamine is effective in supplying fluvoxamine to the blood of a patient such that, following a single application of the composition to the patient, the amount of circulating fluvoxamine ( $AUC_{0-x}$ ) in the blood serum of the patient is about 128 to about 1,175 ng/ml.h.

114. (New) A method for the treatment of depression or obsessive compulsive disorder treatable with an SSRI, comprising administering to a patient suffering from one of the conditions a therapeutically effective amount of a multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) composition for oral administration comprising two quantities of particles, each of the particles comprise

- (i) an inert non-pareil core,
- (ii) an SSRI layer comprising fluvoxamine or a pharmaceutically-acceptable salt thereof disposed over the inert core, and
- (iii) a coating of a rate-controlling polymeric acrylate, methacrylate lacquer, or a mixture thereof disposed over the fluvoxamine,

wherein the composition allows the controlled release of the fluvoxamine over a period of not less than about 12 hours following oral administration, and wherein the rate-controlling polymeric acrylate or methacrylate lacquer coating of the first quantity of particles is present in a first amount, and the rate-controlling polymeric acrylate or methacrylate lacquer coating of the second quantity of particles is present in a second amount that is different from the first amount, and wherein the fluvoxamine release rate from the composition exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

- (a) no more than about 20% of the total fluvoxamine is released after 4 hours of measurement in the apparatus;
- (b) no more than about 45% of the total fluvoxamine is released after 6 hours of measurement in the apparatus;
- (c) between about 45% and 80% of the total fluvoxamine is released after 8 hours of measurement in the apparatus;
- (d) not less than about 70% of the total fluvoxamine is released after 10 hours of measurement in the apparatus; and

(e) not less than about 80% of the total fluvoxamine is released after 12 hours of measurement in the apparatus.

115. (New) A method for the treatment of depression or obsessive compulsive disorder treatable with an SSRI, comprising administering to a patient suffering from one of the conditions a therapeutically effective amount of a multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) composition for oral administration comprising two quantities of particles, each of the particles comprise

(i) an inert non-pareil core,

(ii) an SSRI layer comprising fluvoxamine or a pharmaceutically-acceptable salt thereof disposed over the inert core, and

(iii) a coating of a rate-controlling polymeric acrylate, methacrylate lacquer, or a mixture thereof disposed over the fluvoxamine,

wherein the composition allows the controlled release of the fluvoxamine over a period of not less than about 12 hours following oral administration, and wherein the rate-controlling polymeric acrylate or methacrylate lacquer coating of the first quantity of particles is present in a first amount, and the rate-controlling polymeric acrylate or methacrylate lacquer coating of the second quantity of particles is present in a second amount that is different from the first amount, and wherein the fluvoxamine release rate from the composition exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

(a) no more than 20% of the total fluvoxamine is released after 1 hour of measurement in the apparatus;

(b) no more than 60% of the total fluvoxamine is released after 2 hours of measurement in the apparatus;

(c) not less than 20% of the total fluvoxamine is released after 4 hours of measurement in the apparatus;

(d) not less than 35% of the total fluvoxamine is released after 6 hours of measurement in the apparatus;

(e) not less than 50% of the total fluvoxamine is released after 8 hours of measurement in the apparatus;

(f) not less than 70% of the total fluvoxamine is released after 10 hours of measurement in the apparatus; and

(g) not less than 75% of the total fluvoxamine is released after 12 hours of measurement in the apparatus.

116. (New) A method for the treatment of depression or obsessive compulsive disorder treatable with an SSRI, comprising administering to a patient suffering from one of the conditions a therapeutically effective amount of a multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) composition for oral administration comprising two quantities of particles, each of the particles comprise

- (i) an inert non-pareil core,
- (ii) an SSRI layer comprising fluvoxamine or a pharmaceutically-acceptable salt thereof disposed over the inert core, and
- (iii) a coating of a rate-controlling polymeric acrylate, methacrylate lacquer, or a mixture thereof disposed over the fluvoxamine,

wherein the composition allows the controlled release of the fluvoxamine over a period of not less than about 12 hours following oral administration, and wherein the rate-controlling polymeric acrylate or methacrylate lacquer coating of the first quantity of particles is present in a first amount, and the rate-controlling polymeric acrylate or methacrylate lacquer coating of the second quantity of particles is present in a second amount that is different from the first amount, and wherein the fluvoxamine release rate from the composition exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8: (a) no more than about 20% of the total fluvoxamine is released after 1 hour of measurement in the apparatus;

(b) no more than about 45% of the total fluvoxamine is released after 2 hours of measurement in the apparatus;

(c) between about 20% and about 70% of the total fluvoxamine is released after 4 hours of measurement in the apparatus;

(d) between about 35% and about 85% of the total fluvoxamine is released after 6 hours of measurement in the apparatus;

(e) not less than about 50% of the total fluvoxamine is released after 8 hours of measurement in the apparatus;

(f) not less than about 70% of the total fluvoxamine is released after 10 hours of measurement in the apparatus; and

(g) not less than about 75% of the total fluvoxamine is released after 12 hours of measurement in the apparatus.

117. (New) A method for the treatment of depression or obsessive compulsive disorder treatable with an SSRI, comprising administering to a patient suffering from one of the conditions a therapeutically effective amount of a multiparticulate controlled

release selective serotonin reuptake inhibitor (SSRI) composition for oral administration comprising two quantities of particles, each of the particles comprise

- (i) an inert non-pareil core,
- (ii) an SSRI layer comprising fluvoxamine or a pharmaceutically-acceptable salt thereof disposed over the inert core, and
- (iii) a coating of a rate-controlling polymeric acrylate, methacrylate lacquer, or a mixture thereof disposed over the fluvoxamine,

wherein the composition allows the controlled release of the fluvoxamine over a period of not less than about 12 hours following oral administration, and wherein the rate-controlling polymeric acrylate or methacrylate lacquer coating of the first quantity of particles is present in a first amount, and the rate-controlling polymeric acrylate or methacrylate lacquer coating of the second quantity of particles is present in a second amount that is different from the first amount, and wherein the fluvoxamine release rate from the composition exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

- (a) no more than about 50% of the total fluvoxamine is released after 2 hours of measurement in the apparatus;
- (b) not less than about 35% of the total fluvoxamine is released after 6 hours of measurement in the apparatus; and
- (c) not less than about 80% of the total fluvoxamine is released after 22 hours of measurement in the apparatus.